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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,932	07/18/2003	Subhashis Banerjee	BBI-8187RCE	3572

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LAHIVE & COCKFIELD, LLP
FLOOR 30, SUITE 3000
ONE POST OFFICE SQUARE
BOSTON, MA 02109

EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	PAPER NUMBER
1643	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/622,932	BANERJEE ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,10-14 and 18-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,10-14 and 18-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/28/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 14 April 2008 has been entered.

2. Claims 1-7, 9 and 15-17 have been cancelled.
Claims 8 and 10-14 have been amended.
Claims 18-26 have been added.

3. Claims 8, 10-14 and 18-26 are under consideration.

4. This Office Action contains New Grounds of Rejections

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 28 May 2008 has been fully considered by the examiner. A signed and initialed copy of the IDS is included with the instant Office Action.

Objections/Rejections Withdrawn

6. The rejection of claims 5, 9 and 12 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating psoriasis in a subject comprising administering a human anti-human TNFα antibody or antigen-binding fragment thereof comprising a light chain comprising CDR1 of SEQ ID NO:7, CDR2 of SEQ ID NO:5 and CDR3 of SEQ ID NO:3 comprising the recited amino acid substitutions and a heavy chain comprising CDR1 of SEQ ID NO:8, CDR2 of SEQ ID NO:6 and CDR3 of SEQ ID NO:4 comprising the recited amino acid substitutions, does not reasonably provide enablement for a method of treating psoriasis in a subject comprising administering a human anti-human TNFα antibody or antigen-binding

fragment thereof comprising a light chain comprising CDR3 of SEQ ID NO:3 comprising the recited amino acid substitutions and a heavy chain comprising a heavy chain comprising CDR3 of SEQ ID NO:4 comprising the recited amino acid substitutions as broadly encompassed by the claims is withdrawn in view of the cancellation of claims 5 and 9 and the amendment to claim 12.

7. The rejection of claims 1-2 and 4-14 under 35 U.S.C. 103(a) as being unpatentable over Oh et al (Journal of the American Academy of Dermatology, 42(5):829-830, 2000) in view of Salfeld et al [a] (WO 97/29131, publication date 8/14/1997) is withdrawn in view of the amendments to the claims and the cancellation of claims 1-2 and 9.

8. The rejection of claims 1-2, and 4-14 under 35 U.S.C. 103(a) as being unpatentable over Oh et al (Journal of the American Academy of Dermatology, 42(5):829-830, 2000) in view of Salfeld et al [b] (US Patent 6,509,015 B1, 2/9/1996) is withdrawn in view of the amendments to the claims and the cancellation of claims 1-2 and 9.

9. The rejection of claims 1-2 and 4-14 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 16, 36-39, 48 and 69-70 of U.S. Patent No. 6,509,015 B1 in view of Oh et al (Journal of the American Academy of Dermatology, 42(5):829-830, 2000) is withdrawn in view of the amendments to the claims and the cancellation of claims 1-2 and 9.

10. The provisional rejection of claims 1-2 and 4-14 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 and 73-84 of copending Application No. 10/163,657 in view of Oh et al (Journal of the American Academy of Dermatology, 42(5):829-830, 2000) is withdrawn in view of the amendments to the claims and the cancellation of claims 1-2 and 9.

11. The provisional rejection of claims 1-2, 4-7 and 9 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 and 73-84 of copending Application No. 10/163,657 in view of Oh et al (Journal of the American Academy of Dermatology, 42(5):829-830, 2000) is withdrawn in view of the cancellation of the claims.

12. The provisional rejection of claims 1-2 and 4-14 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 15 of copending Application No. 11/233,252 in view of Oh et al (Journal of the American Academy of Dermatology, 42(5):829-830, 2000) and Salfeld et al [a] (WO 97/29131, publication date 8/14/1997) is withdrawn in view of the amendments to the claims and the cancellation of claims 1-2 and 9.

13. The provisional rejection of claims 1-2, 4-7 and 9 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5,7-26 and 28-53 of copending Application No. 11/104,117 in view of Oh et al (Journal of the American Academy of Dermatology, 42(5):829-830, 2000) is withdrawn in view of the cancellation of the claims.

Objections/Rejections Maintained

14. The objection to the specification as disclosing various non-provisional US Application numbers whose status has changed and require updating is maintained.

The response filed 4/14/2008 submits an amendment updating the status of many of the disclosed non-provisional applications, however, USSN 10/623,076 at pg. 1, should be updated as "now abandoned". Applicants' cooperation is again requested in reviewing the entire disclosure for additional non-provisional U.S. Application Numbers (i.e., USSN 10/623,039 and 10/623,318) that require updating.

Appropriate correction is required.

15. The objection to the title of the invention as not descriptive or clearly indicative of the invention to which the claims are directed is maintained.

The response filed 4/14/2008 states that the title will be amended upon allowance of the claims. Applicants' remarks are acknowledged, however, the claims in the present application are not currently in condition for allowance and the objection is maintained. Applicant should restrict the title to the treatment of psoriasis using human TNFα antibodies.

Appropriate correction is required.

16. The provisional rejection of claims 8, 10-14 and now applied to newly added claims 18-26 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-10, 16-21, 78-79, 81, 84, 86-88, 95, 97-98 and 100-104 of copending Application No. 10/163,657 in view of Oh et al (Journal of the American Academy of Dermatology, 42(5):829-830, 2000) is maintained.

The response filed 4/14/2008 states that the rejection is provisional in nature and will be addressed when appropriate, i.e., when the nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the later-filed application. Applicants' remarks are acknowledged, however, in view that the claims are rejected on other grounds and not presently in condition for allowance, the rejection is maintained.

Applicant is reminded that the U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned copending Application No. 10/163,657, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

17. The provisional rejection of claims 8, 10-14 and now applied to newly added claims 18-25 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 5, 9-22, 25-26 and 28-53 of copending Application No.

11/104,117 in view of Oh et al (Journal of the American Academy of Dermatology, 42(5):829-830, 2000) is maintained.

The response filed 4/14/2008 states that the rejection is provisional in nature and will be addressed when appropriate, i.e., when the nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the later-filed application. Applicants' remarks are acknowledged, however, in view that the claims are rejected on other grounds and not presently in condition for allowance, the rejection is maintained.

Applicant is reminded that the U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned copending Application No. 11/104,117, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

New Grounds of Rejections

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 8, 10-14 and 18-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oh et al (Journal of the American Academy of Dermatology, 42(5):829-830, 2000, cited on PTO-892 mailed 9/6/06) in view of Salfeld et al [a] (WO 97/29131, publication date 8/14/1997, cited on PTO-892 mailed 9/6/06) and Keystone et al ("The Fully Human Anti-TNF Monoclonal Antibody, Adalimumab (D2E7), Dose Ranging Study: The 24-Week Clinical Results in Patients with Active RA on Methotrexate Therapy (The ARMADA Trial)", *Presented at the Annual Meeting of the Against Rheumatoid Arthritis (EULAR), Prague, Czech Republic,* 2001, IDS reference C62 filed 5/28/08).

The claims are drawn to a method of treating psoriasis in a subject comprising biweekly, subcutaneous administration of a unit dosage form comprising 10-150 mg, 20-80 mg or about 40 mg of an anti-TNFα antibody or antigen-binding fragment thereof

such that psoriasis is treated, wherein the anti-TNFα antibody or antigen-binding fragment thereof dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} of 1 x 10^{-3} s^{-1} or less, as determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less, or comprises a light chain variable region comprising SEQ ID NO:1 and a heavy chain variable region comprising SEQ ID NO:2 or the antibody is D2E7, and is administered with one additional therapeutic agent selected from a topical corticosteroid, a vitamin D analog and a topical or oral retinoid.

Oh et al teach a method of treating psoriasis in a patient comprising administering a therapeutically effective amount of a humanized anti-TNFα monoclonal antibody (Infliximab). Oh et al do not specifically teach biweekly, subcutaneous administration of a unit dosage form comprising 10-150 mg, 20-80 mg or about 40 mg of an anti-TNFα antibody or antigen-binding fragment thereof such that psoriasis is treated, wherein the anti-TNFα antibody or antigen-binding fragment thereof dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} of 1 x 10^{-3} s^{-1} or less, as determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less, or comprises a light chain variable region comprising SEQ ID NO:1 and a heavy chain variable region comprising SEQ ID NO:2 or the antibody is D2E7, or administration with one additional therapeutic agent selected from a topical corticosteroid, a vitamin D analog and a topical or oral retinoid. These deficiencies are made up for in the teachings of Salfeld et al [a] and Keystone et al.

Salfeld et al [a] teach that because humanized antibodies still retain some of murine sequence, they still may elicit an unwanted immune reaction in human patients and Salfeld et al [a] teach a method for treating TNFα-related disorders in a subject comprising administering a therapeutically effective amount of the neutralizing, high affinity fully human D2E7 anti-human TNFα antibody or antigen-binding fragment thereof identical to the claimed human anti-human TNFα antibodies, i.e., dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and has a K_{off} of 1 x 10^{-3} s^{-1} or less, as

determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less, and wherein the human antibody or antigen-binding fragment thereof comprises a light chain variable region comprising SEQ ID NO:1 and a heavy chain variable region comprising SEQ ID NO:2 and is administered with one or more additional therapeutic agents, including corticosteroids (see entire document, particularly pp. 2-4, 5-6, 12-15, 29-31 and 35-40). Salfeld also teaches a variety of administration regimens, routes of administration, antibody fragments, antibody heavy chain constant regions, and dosages, such as 0.1-20 mg/kg (see entire document, in particular pp. 33-34). Salfeld also teaches that "[d]osage regimens may be adjusted to provide the optimum desired response (e.g., a therapeutic or prophylactic response). For example, a single bolus may be administered, several divided doses may be administered over time or the dose may be proportionally reduced or increased as indicated by the exigencies of the therapeutic situation… It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that dosage ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed composition (see pp. 33-34). Thus, according to the teaching of Salfeld, *the dosage regimen for anti-TNFα antibody, including dosage scheduling and amount, is a recognized results-effective variable,* i.e., a variable that is recognized as important for therapeutic use of an anti-TNFα antibody and which therefore can be optimized by routine experimentation. See M.P.E.P. § 2144.05 II.B. and *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

Keystone et al teach that the fully human anti- TNFα antibody D2E7 administered subcutaneously at 20 mg, 40 mg and 80 mg every other week (i.e., biweekly) was well tolerated and therapeutically effective, particularly at 40 mg every other week (see entire document).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the neutralizing, high affinity human D2E7

anti-human TNFα antibody or antigen-binding fragments thereof of Salfeld et al [a], and administered subcutaneously every other week at 20 mg, 40 mg or 80 mg (particularly 40 mg) with a corticosteroid for the treatment of psoriasis in a patient as taught by Oh et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to use the neutralizing, high affinity human D2E7 anti-human TNFα antibody or antigen-binding fragments thereof of Salfeld et al [a], and administered subcutaneously every other week at 20 mg, 40 mg or 80 mg (particularly 40 mg) with a corticosteroid for the treatment of psoriasis in a patient in view of Oh et al and Keystone et al because Oh et al teach a method of treating psoriasis in a patient comprising administering a therapeutically effective amount of a humanized anti-TNFα monoclonal antibody (Infliximab), however, Salfeld et al [a] teach that because humanized antibodies still retain some of murine sequence, they still may elicit an unwanted immune reaction in human patients and Salfeld et al [a] teach the neutralizing, high affinity fully human D2E7 anti-human TNFα antibody and antigen-binding fragments thereof for treating TNFα-related disorders in a subject comprising administering a therapeutically effective amount of a human anti-human TNFα antibody or antigen-binding fragment thereof identical to the claimed human anti-human TNFα antibodies, i.e., identical structures/sequences, binding kinetics and neutralization properties (discussed supra) and administered with a corticosteroid and Keystone et al teach that the fully human anti-TNFα antibody D2E7 administered subcutaneously at 20 mg, 40 mg and 80 mg every other week (i.e., biweekly) was well tolerated and therapeutically effective, particularly at 40 mg every other week. Therefore, one of ordinary skill in the art would have been motivated to modify the method of Oh et al using the fully human D2E7 anti-human TNFα antibody and antigen-binding fragments thereof of Salfeld et al [a] in order to avoid any unwanted immune reaction in human patients due to the presence of murine sequences in the humanized anti-TNFα antibody of Oh et al. Additionally, one of ordinary skill in the art would have been motivated to administer the D2E7 antibody or

antigen-binding fragments thereof subcutaneously at 20 mg, 40 mg or 80 mg every other week, which is well tolerated and therapeutically effective according to Keystone et al. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Further, one of ordinary skill in the art would have a reasonable expectation of success in view of the teachings of Oh et al providing evidence that the administration of an anti-TNFα antibody is a clinically effective treatment for psoriasis. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to produce a method of treating psoriasis in a human patient comprising biweekly, subcutaneous administration of the neutralizing, high affinity human D2E7 anti-human TNFα antibody or antigen-binding fragments thereof at 20 mg, 40 mg or 80 mg and administered with a corticosteroid in view of the teachings of Oh et al and Salfeld et al [a] and Keystone et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

20. Claims 18, 10-14 and 18-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oh et al (Journal of the American Academy of Dermatology, 42(5):829-830, 2000, cited on PTO-892 mailed 9/6/06) in view of Salfeld et al [b] (US Patent 6,509,015 B1, 2/9/1996, cited on PTO-892 mailed 9/6/06) and Keystone et al ("The Fully Human Anti-TNF Monoclonal Antibody, Adalimumab (D2E7), Dose Ranging Study: The 24-Week Clinical Results in Patients with Active RA on Methotrexate Therapy (The ARMADA Trial)", *Presented at the Annual Meeting of the Against Rheumatoid Arthritis (EULAR), Prague, Czech Republic,* 2001, IDS reference C62 filed 5/28/08).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The claims have been described supra.

Oh et al have been described supra. Oh et al do not specifically teach biweekly, subcutaneous administration of a unit dosage form comprising 10-150 mg, 20-80 mg or about 40 mg of an anti-TNFα antibody or antigen-binding fragment thereof such that psoriasis is treated, wherein the anti-TNFα antibody or antigen-binding fragment thereof dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} of 1 x 10^{-3} s^{-1} or less, as determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less, or comprises a light chain variable region comprising SEQ ID NO:1 and a heavy chain variable region comprising SEQ ID NO:2 or the antibody is D2E7, or administration with one additional therapeutic agent selected from a topical corticosteroid, a vitamin D analog and a topical or oral retinoid. These deficiencies are made up for in the teachings of Salfeld et al [b] and Keystone et al.

Salfeld et al [b] teach that because humanized antibodies still retain some of murine sequence, they still may elicit an unwanted immune reaction in human patients and Salfeld et al [b] teach a method for treating TNFα-related disorders in a subject comprising administering a therapeutically effective amount of the neutralizing, high affinity fully human D2E7 anti-human TNFα antibody or antigen-binding fragment thereof identical to the claimed human anti-human TNFα antibodies, i.e., dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and has a K_{off} of 1 x 10^{-3} s^{-1} or less, as determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less, and wherein the human antibody or antigen-binding fragment thereof comprises a light chain variable region

comprising SEQ ID NO:1 and a heavy chain variable region comprising SEQ ID NO:2 and is administered with one or more additional therapeutic agents, including corticosteroids (see entire document, particularly columns 2-4, 9-13, 22 and 25). Salfeld [b] also teaches a variety of administration regimens, routes of administration, antibody fragments, antibody heavy chain constant regions, and dosages, such as 0.1-20 mg/kg (see entire document, in particular cols. 22-23). Salfeld [b] also teaches that "[d]osage regimens may be adjusted to provide the optimum desired response (e.g., a therapeutic or prophylactic response). For example, a single bolus may be administered, several divided doses may be administered over time or the dose may be proportionally reduced or increased as indicated by the exigencies of the therapeutic situation… It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that dosage ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed composition (see cols. 22-23). Thus, according to the teaching of Salfeld [b], *the dosage regimen for anti-TNFα antibody, including dosage scheduling and amount, is a recognized results-effective variable,* i.e., a variable that is recognized as important for therapeutic use of an anti-TNFα antibody and which therefore can be optimized by routine experimentation. See M.P.E.P. § 2144.05 II.B. and *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

Keystone et al have been described supra.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the neutralizing, high affinity human D2E7 anti-human TNFα antibody or antigen-binding fragments thereof of Salfeld et al [b], and administered subcutaneously every other week at 20 mg, 40 mg or 80 mg (particularly 40 mg) with a corticosteroid for the treatment of psoriasis in a patient as taught by Oh et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to use the

neutralizing, high affinity human D2E7 anti-human TNFα antibody or antigen-binding fragments thereof of Salfeld et al [b], and administered subcutaneously every other week at 20 mg, 40 mg or 80 mg (particularly 40 mg) with a corticosteroid for the treatment of psoriasis in a patient in view of Oh et al and Keystone et al because Oh et al teach a method of treating psoriasis in a patient comprising administering a therapeutically effective amount of a humanized anti-TNFα monoclonal antibody (Infliximab), however, Salfeld et al [b] teach that because humanized antibodies still retain some of murine sequence, they still may elicit an unwanted immune reaction in human patients and Salfeld et al [b] teach the neutralizing, high affinity fully human D2E7 anti-human TNFα antibody and antigen-binding fragments thereof for treating TNFα-related disorders in a subject comprising administering a therapeutically effective amount of a human anti-human TNFα antibody or antigen-binding fragment thereof identical to the claimed human anti-human TNFα antibodies, i.e., identical structures/sequences, binding kinetics and neutralization properties (discussed supra) and administered with a corticosteroid and Keystone et al teach that the fully human anti-TNFα antibody D2E7 administered subcutaneously at 20 mg, 40 mg and 80 mg every other week (i.e., biweekly) was well tolerated and therapeutically effective, particularly at 40 mg every other week. Therefore, one of ordinary skill in the art would have been motivated to modify the method of Oh et al using the human D2E7 anti-human TNFα antibody or antigen-binding fragments thereof of Salfeld et al [b] in order to avoid any unwanted immune reaction in human patients due to the presence of murine sequences in the humanized anti-TNFα antibody of Oh et al. Additionally, one of ordinary skill in the art would have been motivated to administer the D2E7 antibody or antigen-binding fragments thereof subcutaneously at 20 mg, 40 mg or 80 mg every other week, which is well tolerated and therapeutically effective according to Keystone et al. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702

F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Further, one of ordinary skill in the art would have a reasonable expectation of success in view of the teachings of Oh et al providing evidence that the administration of an anti-TNFα antibody is a clinically effective treatment for psoriasis. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to produce a method of treating psoriasis in a human patient comprising biweekly, subcutaneous administration of the neutralizing, high affinity human D2E7 anti-human TNFα antibody or antigen-binding fragments thereof at 20 mg, 40 mg or 80 mg and administered with a corticosteroid in view of the teachings of Oh et al and Salfeld et al [b] and Keystone et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

21. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

22. Claims 8, 10-14 and 18-25 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 36-39 and 69-70 of U.S. Patent No. 6,509,015 B1 in view of Oh et al (Journal of the American Academy of Dermatology, 42(5):829-830, 2000, cited on PTO-8892 mailed 9/6/06) and Keystone et al ("The Fully Human Anti-TNF Monoclonal Antibody, Adalimumab (D2E7), Dose Ranging Study: The 24-Week Clinical Results in Patients with Active RA on Methotrexate Therapy (The ARMADA Trial)", *Presented at the Annual Meeting of the Against Rheumatoid Arthritis (EULAR), Prague, Czech Republic,* 2001, IDS reference C62 filed 5/28/08).

The instant claims have been described supra.

Claims 1-7, 36-39 and 69-70 of U.S. Patent No. 6,509,015 B1 are drawn to a method of inhibiting human TNFα activity in a human subject and a method of treating a human subject suffering from a disorder in which TNFα activity is detrimental comprising administering to the human subject a human anti-human TNFα antibody or antigen-binding fragment thereof that is identical to the neutralizing, high affinity human anti-human TNFα antibodies and antigen-binding fragments thereof of the present claims, i.e., identical structures/sequences, binding kinetics and neutralization properties and wherein the administered human anti-human TNFα antibody or antigen binding fragment thereof is optionally administered with at least one additional therapeutic agent. Claims 1-7, 36-39 and 69-70 of U.S. Patent No. 6,509,015 B1 do not teach biweekly, subcutaneous administration of a unit dosage form comprising 10-150 mg, 20-80 mg or about 40 mg of the human anti-human TNFα antibody or antigen-binding fragment thereof for the treatment of psoriasis in a human patient. These deficiencies are made up for in the teachings of Oh et al and Keystone et al.

Oh et al have been described supra.

Keystone et al have been described supra.

The claims in the instant application are obvious variants of claims 1-7, 36-39 and 69-70 of U.S. Patent No. 6,509,015 B1 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to

treat psoriasis in a human patient comprising biweekly, subcutaneous administration of the human anti-human TNFα antibodies or an antigen-binding fragment thereof at a dose of 20 mg, 40 mg or 80 mg and optionally with at least one additional therapeutic agent according to claims 1-7, 36-39 and 69-70 of U.S. Patent No. 6,509,015 B1 in view of the teachings of Oh et al and Keystone et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to treat psoriasis in a human patient comprising biweekly, subcutaneous administration of the human anti-human TNFα antibodies or an antigen-binding fragment thereof at a dose of 20 mg, 40 mg or 80 mg and optionally with at least one additional therapeutic agent according to claims 1-7, 36-39 and 69-70 of U.S. Patent No. 6,509,015 B1 in view of the teachings of Oh et al and Keystone et al because Oh et al teach the administration of an anti-TNFα antibody effectively treats psoriasis in a human patient and Keystone et al teach that the fully human anti-TNFα antibody D2E7 administered subcutaneously at 20 mg, 40 mg and 80 mg every other week (i.e., biweekly) was well tolerated and therapeutically effective, particularly at 40 mg every other week. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to treat psoriasis in a human patient comprising biweekly, subcutaneous administration of the human anti-human TNFα antibodies or an antigen-binding fragment thereof at a dose of 20 mg, 40 mg or 80 mg and optionally with at least one additional therapeutic agent according to claims 1-7, 36-39 and 69-70 of U.S. Patent No. 6,509,015 B1 in view of the teachings of Oh et al and Keystone et al.

Claims 8, 10-14 and 18-25 are directed to an invention not patentably distinct from claims 1-7, 36-39 and 69-70 of commonly assigned U.S. Patent No. 6,509,015 B1. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 6,509,015 B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the

commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

23. Claims 8, 10-14 and 18-26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 15 of copending Application No. 11/233,252 (***allowed, not yet issued***) in view of Oh et al (Journal of the American Academy of Dermatology, 42(5):829-830, 2000, cited on PTO-892 mailed 9/6/06) and Salfeld et al [a] (WO 97/29131, publication date 8/14/1997, cited on PTO-892 mailed 9/6/06) and Keystone et al ("The Fully Human Anti-TNF Monoclonal Antibody, Adalimumab (D2E7), Dose Ranging Study: The 24-Week Clinical Results in Patients with Active RA on Methotrexate Therapy (The ARMADA Trial)", *Presented at the Annual Meeting of the Against Rheumatoid Arthritis (EULAR), Prague, Czech Republic,* 2001, IDS reference C62 filed 5/28/08).

The instant claims have been described supra.

Claim 15 of copending Application No. 11/233,252 is drawn to a method for treating a subject suffering from various disorders in which TNFα activity is detrimental comprising administering a pharmaceutical composition comprising an isolated human anti-human TNFα antibody or antigen-binding fragment thereof that dissociates from human TNFα with a K_d of 1×10^{-8} M or less and has a K_{off} of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in

a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less. Claim 15 of copending Application No. 11/233,252 does not specifically teach biweekly, subcutaneous administration of a unit dosage form comprising 10-150 mg, 20-80 mg or about 40 mg of a human anti-human TNFα antibody or antigen-binding fragment thereof for the treatment of psoriasis in a human patient, wherein the antibody comprises the light chain variable region of SEQ ID NO:1 and the heavy chain variable region of SEQ ID NO:2 or wherein the anti-human TNFα antibody is antibody D2E7 and in combination with at least one additional therapeutic agent selected from a topical corticosteroid, a vitamin D analog and a topical or oral retinoid. These deficiencies are made up for in the teachings of Oh et al and Salfeld et al [a] and Keystone et al.

Oh et al have been described supra.

Salfeld et al [a] have been described supra.

Keystone et al have been described supra.

The claims in the instant application are obvious variants of claim 15 of copending Application No. 11/233,252 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to produce a method for treating psoriasis in a human subject comprising biweekly, subcutaneous administering the human D2E7 anti-human TNFα antibodies of Salfeld et al [a] at 20 mg, 40 mg or 80 mg (particularly 40 mg) with a corticosteroid for the treatment of psoriasis in a patient.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to produce a method for treating psoriasis in a human subject comprising biweekly, subcutaneous administering the human D2E7 anti-human TNFα antibodies of Salfeld et al [a] at 20 mg, 40 mg or 80 mg (particularly 40 mg) with a corticosteroid for the treatment of psoriasis in a patient. in view of claim 15 of copending Application No. 11/233,252 and Oh et al and Salfeld et al [a] and Keystone et al because Oh et al teach a method of treating psoriasis in a patient comprising administering a therapeutically effective

amount of a humanized anti-TNFα monoclonal antibody (Infliximab), however, Salfeld et al [a] teach that because humanized antibodies still retain some of murine sequence, they still may elicit an unwanted immune reaction in human patients and Salfeld et al [a] teach the neutralizing, high affinity fully human D2E7 anti-human TNFα antibody and antigen-binding fragments thereof for treating TNFα-related disorders in a subject comprising administering a therapeutically effective amount of a human anti-human TNFα antibody or antigen-binding fragment thereof identical to the human anti-human TNFα antibodies claimed in the present application and administered with a corticosteroid and Keystone et al teach that the fully human anti-TNFα antibody D2E7 administered subcutaneously at 20 mg, 40 mg and 80 mg every other week (i.e., biweekly) was well tolerated and therapeutically effective, particularly at 40 mg every other week. Therefore, one of ordinary skill in the art would have been motivated to modify the method of Oh et al using the human D2E7 anti-human TNFα antibodies and antigen-binding fragments thereof of Salfeld et al [a] in order to avoid any unwanted immune reaction in human patients due to the presence of murine sequences in the humanized anti-TNFα antibody of Oh et al and one of ordinary skill in the art would have been motivated to administer the D2E7 antibody or antigen-binding fragments thereof subcutaneously at 20 mg, 40 mg or 80 mg every other week, which is well tolerated and therapeutically effective according to Keystone et al. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to produce a method for treating psoriasis in a human subject comprising biweekly, subcutaneous administering the human D2E7 anti-human TNFα antibodies of Salfeld et al [a] at 20 mg, 40 mg or 80 mg (particularly 40 mg) with a corticosteroid for the treatment of psoriasis in a patient. in view of claim 15 of copending Application No. 11/233,252 and Oh et al and Salfeld et al [a] and Keystone et al.

Claims 8, 10-14 and 18-26 are directed to an invention not patentably distinct from claim 15 of commonly assigned copending Application No. 11/233,252. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned copending Application No. 11/233,252, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

24. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For

more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643